



*1/16*

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Kiyotaka Nakano et al.                      Art Unit : Unknown  
Serial No. : 10/582,176                                      Examiner : Unknown  
Filed : June 9, 2006                                        Conf. No. : 8936  
Title : METHODS OF SCREENING FOR MODIFIED ANTIBODIES WITH  
AGONISTIC ACTIVITIES

**MAIL STOP AMENDMENT**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

INFORMATION DISCLOSURE STATEMENT

Applicants request consideration of the references listed on the attached PTO-1449 form. Under 37 C.F.R. § 1.98 (a)(2)(ii), only copies of foreign patent documents and/or non-patent literature are enclosed. Copies of any listed U.S. patents or U.S. patent application publications can be provided upon request. Also enclosed are English translations of an International Search Report and an International Preliminary Report on Patentability (both from PCT/JP2004/018499).

English translations of foreign language references A17-A22, A38, and A39 are not included, since they are members of the patent family of U.S. references A1, A23, A7, A4, A27, A30, A9, and A11, respectively. English translations of references A42-A44 and A79 are provided herewith. In addition, Applicants enclose a concise English explanation of reference A81.

Applicants wish to bring to the Examiner's attention co-pending and co-owned non-provisional application serial numbers 10/530,696 (Attorney Docket No. 14875-141US1), 10/548,727 (Attorney Docket No. 14875-150US1), 10/550,934 (Attorney Docket No. 14875-151US1), 10/551,504 (Attorney Docket No. 14875-153US1), 10/582,413 (Attorney Docket

CERTIFICATE OF MAILING BY FIRST CLASS MAIL

I hereby certify under 37 CFR §1.8(a) that this correspondence is being deposited with the United States Postal Service as first class mail with sufficient postage on the date indicated below and is addressed to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

April 18, 2007  
Date of Deposit

*Scott Barrett*  
Signature

Scott Barrett  
Typed or Printed Name of Person Signing Certificate

Applicant : Kiyotaka Nakano et al.  
Serial No. : 10/582,176  
Filed : June 9, 2006  
Page : 2 of 2

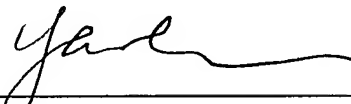
Attorney's Docket No.: 14875-163US1 / C1-A0322P-US

No. 14875-164US1), 10/582,304 (Attorney Docket No. 14875-166US1), 11/547,747 (Attorney Docket No. 14875-171US1), and 10/582,654, which concern related subject matter, and some of which have overlapping inventorship with the above-referenced application. Applicants assume that the Examiner has ongoing access to the files of these related applications and can obtain copies of prosecution documents from the files if at any point in the future he/she considers it potentially relevant to issues in the present application. Applicants will supply copies of such documents from the related applications' files, should the Examiner request them.

This statement is being filed before the receipt of a first Office Action on the merits. Please apply any charges or credits to Deposit Account No. 06-1050, referencing Attorney Docket No. 14875-163US1.

Respectfully submitted,

Date: 4/18/07

 *Reg. No. 34,819*  
for Janis K. Fraser, Ph.D., J.D.  
Reg. No. 34,819

Fish & Richardson P.C.  
225 Franklin Street  
Boston, MA 02110  
Telephone: (617) 542-5070  
Facsimile: (617) 542-8906

Substitute Form PTO-1449

U.S. Department of Commerce  
Patent and Trademark Office

Attorney's Docket No.

14875-163US1

Application No.

10/582,176

**Information Disclosure Statement  
by Applicant**

(Use several sheets if necessary)

(37 CFR 1.98(b))

Applicant

Kiyotaka Nakano et al.

Filing Date

June 9, 2006

Group Art Unit

Unknown

**U.S. Patent Documents**

Examiner Initial	Desig. ID	Document Number	Publication Date	Patentee	Class	Subclass	Filing Date If Appropriate
	A1	5,877,291	04/20/1995	Mezes et al.			
	A2	6,183,744	02/06/2001	Goldenberg			
	A3	6,323,000	11/07/2001	Briggs et al.			
	A4	6,342,220	01/29/2002	Adams et al.			
	A5	6,368,596	04/09/2002	Ghetie et al.			
	A6	6,683,157	01/27/2004	Briggs et al.			
	A7	2001/0006796	07/05/2001	Briggs et al.			
	A8	2002/0193571	12/19/2002	Carter et al.			
	A9	2003/0073161	04/17/2003	Briggs et al.			
	A10	2003/0148409	08/07/2003	Rossi et al.			
	A11	2004/0091475	05/13/2004	Tsuchiya et al.			
	A12	2004/0242847	12/02/2004	Fukushima et al.			
	A13	2006/0189794	08/24/2006	Tsuchiya et al.			
	A14	2006/0222643	10/05/2006	Tsunoda et al.			
	A15	2006/0275301	12/07/2006	Ozaki et al.			
	A16	2007/0003556	01/07/2007	Tsuchiya et al.			

**Foreign Patent Documents or Published Foreign Patent Applications**

Examiner Initial	Desig. ID	Document Number	Publication Date	Country or Patent Office	Class	Subclass	Translation	
							Yes	No
	A17	JP 7-503622	04/20/1995	Japan			See A1	
	A18	JP 10-505231	05/26/1998	Japan			See A23	
	A19	JP 2001-506135	05/15/2001	Japan			See A7	
	A20	JP 2001-513999	09/11/2001	Japan			See A4	
	A21	JP 2001-518930	10/16/2001	Japan			See A27	
	A22	JP 2002-544173	12/24/2002	Japan			See A30	
	A23	WO 96/04925	02/22/1996	WIPO				
	A24	WO 97/31108	08/28/1997	WIPO			English abstract	

Examiner Signature

Date Considered

EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Substitute Form PTO-1449 (Modified)	U.S. Department of Commerce Patent and Trademark Office	Attorney's Docket No. 14875-163US1	Application No. 10/582,176
<b>Information Disclosure Statement by Applicant</b> (Use several sheets if necessary) (37 CFR §1.98(b))		Applicant Kiyotaka Nakano et al.	
		Filing Date June 9, 2006	Group Art Unit Unknown

Foreign Patent Documents or Published Foreign Patent Applications								
Examiner Initial	Desig. ID	Document Number	Publication Date	Country or Patent Office	Class	Subclass	Translation	
							Yes	No
	A25	WO 98/28331	07/02/1998	WIPO				
	A26	WO 98/41641	09/24/1998	WIPO				
	A27	WO 98/42378	10/01/1998	WIPO				
	A28	WO 99/02567	01/21/1999	WIPO				
	A29	WO 99/10494	03/04/1999	WIPO				
	A30	WO 00/67795	11/16/2000	WIPO				
	A31	WO 01/64713	09/07/2001	WIPO				
	A32	WO 01/66737	09/13/2001	WIPO				
	A33	WO 01/74388	10/11/2001	WIPO				
	A34	WO 01/79494	10/25/2001	WIPO			English abstract	
	A35	WO 01/97858	12/27/2001	WIPO				
	A36	WO 02/04021	01/17/2002	WIPO				
	A37	WO 02/22212	03/21/2002	WIPO				
	A38	WO 02/33072	04/25/2002	WIPO			See A9	
	A39	WO 02/33073	04/25/2002	WIPO			See A11	
	A40	WO 03/033654	04/24/2003	WIPO				
	A41	WO 03/104425	12/18/2003	WIPO				
	A42	WO 2004/033499	04/22/2004	WIPO			X	
	A43	WO 2004/081048	09/23/2004	WIPO			X	
	A44	WO 2004/087763	10/14/2004	WIPO			X	

Other Documents (include Author, Title, Date, and Place of Publication)		
Examiner Initial	Desig. ID	Document
	A45	Ballmaier et al., "c-mpl mutations are the cause of congenital amegakaryocytic thrombocytopenia," <i>Blood</i> , 97:139-146 (2001)
	A46	Brinkmann et al., "FTY720: targeting G-protein-coupled receptors for sphingosine 1-phosphate in transplantation and autoimmunity," <i>Curr. Opin. Immunol.</i> , 14:569-575 (2002)
	A47	Bruenke et al., "A recombinant bispecific single-chain Fv antibody against HLA class II and FcγRIII (CD16) triggers effective lysis of lymphoma cells," <i>Br. J. Haematol.</i> , 125:167-179 (2004)

Examiner Signature	Date Considered
EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	

Substitute Form PTO-1449 (Modified)	U.S. Department of Commerce Patent and Trademark Office	Attorney's Docket No. 14875-163US1	Application No. 10/582,176
<b>Information Disclosure Statement by Applicant</b> (Use several sheets if necessary) (37 CFR §1.98(b))		Applicant Kiyotaka Nakano et al.	
		Filing Date June 9, 2006	Group Art Unit Unknown

Other Documents (include Author, Title, Date, and Place of Publication)		
Examiner Initial	Desig. ID	Document
	A48	Clark, "CD22, a B Cell-Specific Receptor, Mediates Adhesion and Signal Transduction," <i>J. Immunol.</i> , 150:4715-4718 (1993)
	A49	Co et al., "A Humanized Antibody Specific for the Platelet Integrin gpIIb/IIIa," <i>J. Immunol.</i> , 152:2968-2976 (1994)
	A50	Daniel et al., "Induction of Apoptosis in Human Lymphocytes by Human Anti-HLA Class I Antibodies," <i>Transplantation</i> , 75:1380-1386 (2003)
	A51	De Felice et al., "Differential regulatory role of monomorphic and polymorphic determinants of histocompatibility leukocyte antigen class I antigens in monoclonal antibody OKT3-induced T cell proliferation," <i>J. Immunol.</i> , 139:2683-2689 (1987)
	A52	DeNardo et al., "Anti-HLA-DR/anti-DOTA Diabody Construction in a Modular Gene Design Platform: Bispecific Antibodies for Pretargeted Radioimmunotherapy," <i>Cancer Biother. Radiopharm.</i> , 16:525-535 (2001)
	A53	Deng et al., "An Agonist Murine Monoclonal Antibody to the Human c-Mpl Receptor Stimulates Megakaryocytopoiesis," <i>Blood</i> , 92:1981-1988 (1998)
	A54	Ebert et al., "Expression of Metallothionein II in Intestinal Metaplasia, Dysplasia, and Gastric Cancer," <i>Cancer Res.</i> , 60:1995-2001 (2000)
	A55	Elliott et al., "Activation of the Erythropoietin (EPO) Receptor by Bivalent Anti-EPO Receptor Antibodies," <i>J. Biol. Chem.</i> , 271:24691-24697 (1996)
	A56	Fayen et al., "Negative signaling by anti-HLA class I antibodies is dependent upon two triggering events," <i>Int. Immunol.</i> , 10:1347-1358 (1998)
	A57	Funaro et al., "Monoclonal antibodies and therapy of human cancers," <i>Biotechnol. Adv.</i> , 18:385-401 (2000)
	A58	Genestier et al., "Antibodies to HLA Class I $\alpha 1$ Domain Trigger Apoptosis of CD40-Activated Human B Lymphocytes," <i>Blood</i> , 90:726-735 (1997)
	A59	Genestier et al., "Caspase-dependent Ceramide Production in Fas- and HLA Class I-mediated Peripheral T Cell Apoptosis," <i>J. Biol. Chem.</i> , 273:5060-5066 (1998)
	A60	Genestier et al., "Fas-Independent Apoptosis of Activated T Cells Induced by Antibodies to the HLA Class I $\alpha 1$ Domain," <i>Blood</i> , 90:3629-3639 (1997)
	A61	Genestier et al., "T cell sensitivity to HLA class I-mediated apoptosis is dependent on interleukin-2 and interleukin-4," <i>Eur. J. Immunol.</i> , 27:495-499 (1997)
	A62	Ghetie et al., "Homodimerization of tumor-reactive monoclonal antibodies markedly increases their ability to induce growth arrest or apoptosis of tumor cells," <i>Proc. Natl. Acad. Sci. USA</i> , 94:7509-7514 (1997)
	A63	Goel et al., " <sup>99m</sup> Tc-Labeled Divalent and Tetravalent CC49 Single-Chain Fv's: Novel Imaging Agents for Rapid In Vivo Localization of Human Colon Carcinoma," <i>J. Nucl. Med.</i> , 42:1519-1527 (2001)
	A64	Goel et al., "Genetically Engineered Tetravalent Single-Chain Fv of the Pancarcinoma Monoclonal Antibody CC49: Improved Biodistribution and Potential for Therapeutic Application," <i>Cancer Res.</i> , 60:6964-6971 (2000)
	A65	Goto et al., "A Novel Membrane Antigen Selectively Expressed on Terminally Differentiated Human B Cells," <i>Blood</i> , 84:1922-1930 (1994)
	A66	Holliger et al., "'Diabodies': Small bivalent and bispecific antibody fragments," <i>Proc. Natl. Acad. Sci. USA</i> , 90:6444-6448 (1993)

Examiner Signature	Date Considered
EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	

Substitute Form PTO-1449 (Modified)	U.S. Department of Commerce Patent and Trademark Office	Attorney's Docket No. 14875-163US1	Application No. 10/582,176
<b>Information Disclosure Statement by Applicant</b> (Use several sheets if necessary)  (37 CFR §1.98(b))		Applicant Kiyotaka Nakano et al.	
		Filing Date June 9, 2006	Group Art Unit Unknown

Other Documents (include Author, Title, Date, and Place of Publication)		
Examiner Initial	Desig. ID	Document
	A67	Hu et al., "Minibody: A Novel Engineered Anti-Carcinoembryonic Antigen Antibody Fragment (Single-Chain Fv-C <sub>H</sub> 3) Which Exhibits Rapid, High-Level Targeting of Xenografts," <i>Cancer Res.</i> , 56:3055-3061 (1996)
	A68	Hudson et al., "High avidity scFv multimers; diabodies and triabodies," <i>J. Immunol. Methods</i> , 231:177-189 (1999)
	A69	Kimura et al., "2D7 diabody bound to the $\alpha 2$ domain of HLA class I efficiently induces caspase-independent cell death against malignant and activated lymphoid cells," <i>Biochem. Biophys. Res. Commun.</i> , 325:1201-1209 (2004)
	A70	Kipriyanov et al., "Effect of Domain Order on the Activity of Bacterially Produced Bispecific Single-chain Fv Antibodies," <i>J. Mol. Biol.</i> , 330:99-111 (2003)
	A71	Kortt et al., "Dimeric and trimeric antibodies: high avidity scFvs for cancer targeting," <i>Biomol. Eng.</i> , 18:95-108 (2001)
	A72	Kreitman et al., "Cytotoxic Activity of Disulfide-stabilized Recombinant Immunotoxin RFB4(dsFv)-PE38 (BL22) toward Fresh Malignant Cells from Patients with B-Cell Leukemias," <i>Clin. Cancer Res.</i> , 6:1476-1487 (2000)
	A73	Kulkarni et al., "Construction of a Single-Chain Antibody Derived From 5H7, A Monoclonal Antibody Specific for a Death Signaling Domain of Human Class I Major Histocompatibility Complex," <i>Transplant. Proc.</i> , 30:1081 (1998)
	A74	Kulkarni et al., "Programmed Cell Death Signaling Via Cell-Surface Expression of a Single-Chain Antibody Transgene," <i>Transplantation</i> , 69:1209-1217 (2000)
	A75	Lebrun et al., "Antibodies to the Extracellular Receptor Domain Restore the Hormone-insensitive Kinase and Conformation of the Mutant Insulin Receptor Valine 382," <i>J. Biol. Chem.</i> , 268:11272-11277 (1993)
	A76	Li et al., "The Epitope Specificity and Tissue Reactivity of Four Murine Monoclonal Anti-CD22 Antibodies," <i>Cell. Immunol.</i> , 118:85-99 (1989)
	A77	Matsuoka et al., "A Monoclonal Antibody to the $\alpha 2$ Domain of Murine Major Histocompatibility Complex Class I that Specifically Kills Activated Lymphocytes and Blocks Liver Damage in the Concanavalin A Hepatitis Model," <i>J. Exp. Med.</i> , 198:497-503 (2003)
	A78	Matsuoka et al., "A Novel Type of Cell Death of Lymphocytes Induced by a Monoclonal Antibody without Participation of Complement," <i>J. Exp. Med.</i> , 181:2007-2015 (1995)
	A79	Nishii, "CD22 antibody therapy," <i>Current Therapy</i> , 20:47-50 (2001) (English translation included)
	A80	Ohtomo et al., "Molecular Cloning and Characterization of a Surface Antigen Preferentially Overexpressed on Multiple Myeloma Cells," <i>Biochem. Biophys. Res. Commun.</i> , 258:583-591 (1999)
	A81	Oka, "Development of Novel Immunotoxin Using Recombinant Alpha-Sarcin and Its Application Treatment of Hematopoietic Tumor," <i>Sankyo Seimei Kagaku Kenkyu Shinko Zaidan Kenkyu Hokokushu</i> , 12:46-56 (1998) (concise English explanation included)
	A82	Ono et al., "The humanized anti-HM1.24 antibody effectively kills multiple myeloma cells by human effector cell-mediated cyto-toxicity," <i>Mol. Immunol.</i> , 36:387-395 (1999)
	A83	Orita et al., "A novel therapeutic approach for thrombocytopenia by minibody agonist of the thrombopoietin receptor," <i>Blood</i> , 105:562-566 (2005)
	A84	Ozaki et al., "A Recombinant HLA Class I-Specific Single Chain Fv Diabody Induces Cell Death in Human Lymphoid Malignancies," <i>Blood</i> , 102:933a, Abstract No. 3474 (2003)

Examiner Signature	Date Considered
EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	

Substitute Form PTO-1449 (Modified)	U.S. Department of Commerce Patent and Trademark Office	Attorney's Docket No. 14875-163US1	Application No. 10/582,176
<b>Information Disclosure Statement by Applicant</b> (Use several sheets if necessary) (37 CFR §1.98(b))		Applicant Kiyotaka Nakano et al.	
		Filing Date June 9, 2006	Group Art Unit Unknown

Other Documents (include Author, Title, Date, and Place of Publication)		
Examiner Initial	Desig. ID	Document
	A85	Ozaki et al., "Humanized Anti-HM1.24 Antibody Mediates Myeloma Cell Cytotoxicity That Is Enhanced by Cytokine Stimulation of Effector Cells," <i>Blood</i> , 93:3922-3930 (1999)
	A86	Ozaki et al., "Immunotherapy of Multiple Myeloma With a Monoclonal Antibody Directed Against a Plasma Cell-Specific Antigen, HM1.24," <i>Blood</i> , 90:3179-3186 (1997)
	A87	Pettersen et al., "The TCR-Binding Region of the HLA Class I $\alpha_2$ Domain Signals Rapid Fas-Independent Cell Death: A Direct Pathway for T Cell-Mediated Killing of Target Cells?" <i>J. Immunol.</i> , 160:4343-4352 (1998)
	A88	Plückthun et al., "New protein engineering approaches to multivalent and bispecific antibody fragments," <i>Immunotechnology</i> , 3:83-105 (1997)
	A89	Rossi et al., "Development of New Multivalent-bispecific Agents for Pretargeting Tumor Localization and Therapy," <i>Clin. Cancer Res.</i> , 9:3886s-3896s (2003)
	A90	Sato et al., "CD22 Is Both a Positive and Negative Regulator of B Lymphocyte Antigen Receptor Signal Transduction: Altered Signaling in CD22-Deficient Mice," <i>Immunity</i> , 5:551-562 (1996)
	A91	Scheurle et al., "Cancer Gene Discovery Using Digital Differential Display," <i>Cancer Res.</i> , 60:4037-4043 (2000)
	A92	Smith et al., "Inhibition of T Cell Activation by a Monoclonal Antibody Reactive Against the $\alpha_3$ Domain of Human MHC Class I Molecules," <i>J. Immunol.</i> , 153:1054-1067 (1994)
	A93	Tahtis et al., "Biodistribution Properties of <sup>111</sup> Indium-labeled C-Functionalized <i>trans</i> -Cyclohexyl Diethylenetriaminepentaacetic Acid Humanized 3S193 Diabody and F(ab') <sub>2</sub> Constructs in a Breast Carcinoma Xenograft Model," <i>Clin. Cancer Res.</i> , 7:1061-1072 (2001)
	A94	Tedder et al., "CD22, a B Lymphocyte-Specific Adhesion Molecule That Regulates Antigen Receptor Signaling," <i>Annu. Rev. Immunol.</i> , 15:481-504 (1997)
	A95	Thilenius et al., "Agonist antibody and Fas ligand mediate different sensitivity to death in the signaling pathways of Fas and cytoplasmic mutants," <i>Eur. J. Immunol.</i> , 27:1108-1114 (1997)
	A96	Woodle et al., "Anti-Human Class I $\alpha_3$ Domain-Specific Monoclonal Antibody Induces Programmed Cell Death in Murine Cells Expressing Human Class I MHC Transgenes," <i>Transplant. Proc.</i> , 30:1059-1060 (1998)
	A97	Woodle et al., "Anti-Human Class I MHC Antibodies Induce Apoptosis by a Pathway That Is Distinct from the Fas Antigen-Mediated Pathway," <i>J. Immunol.</i> , 158:2156-2164 (1997)
	A98	Woodle et al., "Class I MHC Mediates Programmed Cell Death in Human Lymphoid Cells," <i>Transplantation</i> , 64:140-146 (1997)
	A99	Wu et al., "Tumor localization of anti-CEA single-chain Fvs: improved targeting by non-covalent dimers," <i>Immunotechnology</i> , 2:21-36 (1996)
	A100	Xiong et al., "Efficient inhibition of human B-cell lymphoma xenografts with an anti-CD20 $\times$ anti-CD3 bispecific diabody," <i>Cancer Lett.</i> , 177:29-39 (2002)
	A101	Xu et al., "Insight into hepatocellular carcinogenesis at transcriptome level by comparing gene expression profiles of hepatocellular carcinoma with those of corresponding noncancerous liver," <i>Proc. Natl. Acad. Sci. USA</i> , 98:15089-15094 (2001)

Examiner Signature	Date Considered
EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	